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Health and Environmental Effects Profile for Propionitrile

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16. ABSTRACT

The Health and Environmental Effects Profile for propionitrile was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine an Acceptable Daily Intake (ADI) or a carcinogenic potency factor for propionitrile.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a relase as specified by CERCLA based on chronic toxicity. Existing data are insufficient to determine an RQ value.

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR PROPIONITRILE

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1984.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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LIST OF ABBREVIATIONS

ACTH	Adrenocorticotropic hormone
ADI	Acceptable daily intake
BCF	Bioconcentration factor
CAS	Chemical Abstract Service
CNS	Central nervous system
GC	Gas chromatography
K_{oc}	Soil partition coefficient
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients (and all other subscripted concentration levels)
LD_{50}	Dose lethal to 50% of recipients (and all other subscripted dosage levels)
MED	Minimum effective dose
MS	Mass spectrometry
ppm	Parts per million
RQ	Reportable quantity
TLV	Threshold limit value
TWA	Time-weighted average

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

The chemical commonly known as propionitrile is also known by the synonyms ethyl cyanide, propanenitrile, cyanoethane, hydrocyonic ether, propionic nitrile and propylnitrile. Current CAS usage is propanenitrile. The structure of propionitrile is given below:

$$CH_3CH_2CN$$

Empirical formula: C_3H_5N

Molecular weight: 55.08

The CAS Registry number for this compound is 107-12-0.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Propionitrile is a mobile, colorless liquid (Hawley, 1981) with a pleasant, ethereal, sweetish odor (Windholz, 1976). Some of the evidable physical properties of commercially significant 2-ethoxyethanol esters are listed below (Hawley, 1981; Windholz, 1976; Weast, 1980; Sax, 1979; unless otherwise noted):

Melting point:	-91.8°C
Boiling point:	97.2°C (760 mm Hg) 77.7°C (400 mm Hg) 22.0°C (40 mm Hg)
Density:	0.7818 at 20°/4°C
Vapor pressure:	40 mm Hg at 23°C (U.S. EPA, 1985a)
Vapor density:	1.9 (air = 1)
Flash point:	16.1°C (open cup)
Flammability:	quite flammable (U.S. EPA, 1985a)
Explosiveness:	Container may explode in heat of fire; vapor explosion hazardous indoors, outdoors or in sewers; explosive limit, lower: 3.1% (U.S. EPA, 1985a)

Water solubility:	105,000 ppm at 20-25°C (Hansch et al., 1968)
	120,000 ppm (temperature not specified) (Valvani et al., 1981)
	106,000 ppm at 40°C (U.S. EPA, 1985a)
Solubility in other solvents:	Miscible with ethyl alcohol, ethyl ether, dimethylformamide; soluble in acetone, benzene and organic solvents in general
Refractive index:	1.3655 at 20°C
Log K_{OW}:	0.16 (Hansch and Anderson, 1967)
Log K_{OC}:	1.46 (estimated for K_{OW} using Equation 4-8 in Lyman et al., 1982)
BCF:	0.78 (estimated from K_{OW} using equation 5-2 in Lyman et al., 1982)
Henry's Law Constant (H^1) (concentration gas/concentration water) at 25°C	1.51×10^{-8} (Hine and Mookerjee, 1975)
	1.6×10^{-8} (estimated, Section 2.1.)
	1.1×10^{-8} (estimated, Section 2.1.)

1.3. PRODUCTION DATA

Nearly all the propionitrile produced commercially in the United States is formed as a byproduct by electro-reduction of acrylonitrile during the manufacture of adiponitrile by the Monsanto Company (Cazzulino, 1981; U.S. EPA, 1985b). Small amounts of propionitrile are also formed as byproducts in the production of acrylamide from acrylonitrile (MacWilliams, 1978) and in the production of hydrogen cyanide from ammonia (Jenks, 1978). Propionitrile can also be synthesized by dehydration of propionamide and by ethylation of cyanide ion (Windholz, 1976).

Monsanto was the major United States manufacturer listed in U.S. EPA (1985b), with 10-50 million pounds produced at the Decatur, AL, production facility. Other Monsanto facilities were located in Texas City, TX, with a production of 100,000 to 1 million pounds, and at Alvin, TX. Other small scale producers and importers of propionitrile included the following: Longa, Inc., Fair Lawn, NJ; Henley and Co., Inc., New York, NY; Vega, Subsidiary of Kalama Chem., Beaufort, SC; Enenco Inc., Memphis, TN; and American Hoechst Corpora- tion, Bridgewater, NJ (U.S. EPA, 1985b). According to Beaver (1984), Monsanto Co. is the only current bulk producer of propionitrile in the United States.

1.4. USE DATA

Monsanto (Keating, 1981) reported that propionitrile "has a very limited market in which it is used as a chemical intermediate.....If production exceeds the limited market demand, unsold material is incinerated on-site." This is supported by the U.S. EPA (1985b), who noted that the 10-50 million pounds produced at Decatur, AL, were site-limited and that <1 million pounds were shipped off-site. Currently, Monsanto Co. has discontinued incineration of its unsold material. It incinerates only the materials that are out of specification (Beaver, 1984).

Propionic acid can be made from acid hydrolysis of the propionitrile, but that process is not currently used in the United States for the manufacture of propionic a[illegible] (Beaver, 1984).

Acrylonitrile can also be made by dehydration of propionitrile at high temperatures using either an oxide of chromium or vanadium or iodine in the presence of oxygen (Groet, 1978). Other uses reported for propionitrile are as a solvent, a dielectric fluid, an intermediate, a raw material for medicine and a setting agent for resins (Hawley, 1981; U.S. EPA, 1985a).

2. ENVIRONMENTAL FATE AND TRANSPORT

2.1. AIR

Harris et al. (1981) reported that the rate constant for the reaction of propionitrile with hydroxyl radicals at 25°C was, 1.94 ($\pm$0.20)x10^{-13} cm^3 $molecule^{-1}$ sec^{-1}, and the reaction exhibited no dependence upon total pressure. Thus, this reaction may be used to calculate its tropospheric destruction rate which is due to a reaction with OH as ~2x10^{-6} sec^{-1}, assuming a mean tropospheric concentration of 10^7 OH radicals cm^{-3} at 25°C. The reaction of propionitrile with OH radicals proceeds largely or entirely by abstraction of a hydrogen atom. Pitts (1981) measured a rate constant of <1.0x10^{-19} cm^3 $molecule^{-1}$ sec^{-1} for the reaction of propionitrile with ozone. Therefore, the major homogeneous loss process for propionitrile in the atmosphere is expected to be reaction with OH radicals (Harris et al., 1981). A reported estimated lifetime for propionitrile following release into a moderately polluted troposphere is ~6 days.

Direct photolysis of propionitrile is not expected to be significant, as it does not exhibit absorption at $\geq$290 nm (Silverstein et al., 1981); the reported π-π^* absorption for isolated nitriles chromophores is reported to occur at <160 nm.

Pertinent data regarding the dry or wet deposition of propionitrile were not located in the available literature as cited in the Appendix.

Proprionitrile is expected to be oxidized relatively rapidly by the hydroxyl radical in the troposphere. Essentially the same conclusions were reported by the U.S. EPA (1983).

2.2. WATER

Hydrolysis of the cyano group of propionitrile is expected to be very slow under environmental conditions (U.S. EPA, 1983).

Photolysis of propionitrile in water is expected to be negligible because absorption does not occur at ≥290 nm (Silverstein et al., 1981)(see Section 2.1.).

DiGeronimo and Antoine (1976) reported that the fungal strain, Nocardia rhodochrous LL100-21, completely hydrolyzed propionitrile to propionic acid and ammonia. Traces of propionamide were also detected in the culture medium at the end of the incubation period. Propionic acid and propionamide were reported to be detected at 6 hours and their levels increased steadily for the remainder of the growth period in a mole ratio of ~1:1. Collins and Knowles (1983) reported that N. rhodochrous LL100-21 grew with propionitrile as the sole carbon and nitrogen sources, as well as with propionitrile as the sole carbon source with ammonium chloride as the N source, and with propionitrile as the sole nitrogen source with succinate as the carbon source.

Jallageas et al. (1979) reported that the enzyme, nitrilase, hydrolytically degrades nitriles to the corresponding amides. Then the enzyme, amidase, if present, converts the amides to the acids and ammonia.

Propionitrile has also been used as the sole carbon and nitrogen source by the bacteria, Rhodococcus, from soil (Miller and Gray, 1982). The rate of hydrolysis of propionitrile and its initial biodegradation product, propionamide, were shown to be 2.1±0.1 and 9100±1200 nmol ammonia produced/min/mg dry weight of cells, respectively. Kuwahara et al. (1980a) reported that the fungal strain, Fusarium solani MN7030, isolated from a soil sample and cultured in the laboratory, also used propionitrile as a source of carbon and nitrogen for growth. Kuwahara et al. (1980b) reported that growth of Aeromonas sp. BN 7013 was supported by propionitrile.

Yamada et al. (1979) demonstrated that the bacterial strain of Anthrobacter, isolated from acclimated sludge, grew well when propionitrile was used as the sole carbon and nitrogen source. Symons et al. (1961) reported that propionitrile was biologically degradable by activated sludge and that ammonia was released into solution during metabolism. While these data from activated sludge and sludge derived species may not be directly relevant to biodegradation in water, they do help to illustrate the potential for the biodegradation of propionitrile in water.

Propionitrile is not expected to bioconcentrate based on its very low estimated BCF value of 0.78 (see Section 1.2.), especially in view of its susceptibility to biodegradation.

Volatilization of propionitrile from shale oil wastewaters was reported to be a potential source of atmospheric release (Hawthorne and Sievers, 1984). Table 2-1 lists the results of propionitrile volatilization from three separate shale oil processing sites. Only small amounts of propionitrile (ng/mL of compound in air above 1 mL water) were emitted from the wastewaters equilibrated in a closed container (headspace analysis). The purge and trap analysis, however, reveals that wastewaters exposed to large amounts of air emit much higher amounts of propionitrile (μg/mL of wastewater) than an equal amount of the same wastewater held in a closed container with an air headspace of equal volume. As expected, the gas condensate waters generally contained higher proportions of propionitrile than did the process retort water. Propionitrile was detected but not quantified in two samples of ambient air collected in and near the oil shale wastewater treatment facility at the Logan, WA, site of Occidental Oil Shale Inc. It was also stated that unless the shale oil wastewaters are treated to remove volatile contaminants (including propionitrile) before reuse or

TABLE 2-1

Emission of Organic Air Pollutants from Shale Oil Wastewaters[a]

Site[b]	Headspace Analysis[c]		Purge and Trap Analysis[d]	
	Retort Water	Gas Condensate	Retort Water	Gas Condensate
A	ND	ND	2.0	0.11
B	2.2	7.0	4.1	13
C	<1.6	13	1.7	5.7

[a]Source: Hawthorne and Sievers, 1984

[b]A: Rio Blanco Oil Shale Co. (modified in situ) retort 1 burn

B: Laramie Energy Technology Center (experimental 150 ton retort)

C: Occidental Oil Shale Inc., Logan, WA site (recycle mode of modified in situ retorts 7 and 8)

[c]Propionitrile present in the air above shale oil wastewaters in a closed system (ng/mL of air above 1 mL of water)

[d]Propionitrile emitted from shale oil wastewaters during purge and trap anaylsis (μg emitted/mL of wastewater)

ND = Not detected by GC/MS; detection limits ~0.5-1.0 ng/mL headspace

disposal, the emission of these substances could result in a source of air pollutants that is difficult to control. This would be so particularly if the wastewaters are widely distributed, as in proposed codisposal in open fields with retorted spent shale.

The Henry's Law constant (H^1) is defined as the ratio of the concentration of a substance in the gas phase (Cg) to the concentration in the aqueous phase (Cw): H^1=Cg/Cw (equation 15-3, Lyman et al., 1982). The Henry's Law constant is useful to help estimate the rate of volatilization of the substance from a dilute solution in water. It can be derived from reported data concerning the vapor pressure of the substance in equilibrium with a particular known concentration of the substance in water solution. The Henry's nondimensional constant derived for propionitrile using the data reported in Hine and Mookerjee (1975) is 1.51×10^{-3}. A value of 1.6×10^{-3} from Henry's Law constant was calculated using the primary data reported by Butler and Ramchandani (1935). The Henry's Law constant can also be estimated from the vapor pressure (P_{vp}) and solubility (S) of the substance: $H=P_{vp}/S$ (equation 15-8, Lyman et al., 1982). The value of this dimensional Henry's Law constant was found to be 2.8×10^{-3} atm-m³/mol using values of Pvp=40 mm Hg at 23°C (=40 mm Hg at 25°C; U.S. EPA, 1985a) and S=105 g/l (Hansch et al., 1968). This dimensional H is related to the above defined nondimensional H^1 by the equation: $H^1=H/RT=H/0.0245$ at 25°C (Lyman et al., 1982); therefore, $H^1=1.1 \times 10^{-3}$ using the above data.

The Henry's Law constant can be used to estimate the half-life of evaporation of a substance in a body of water. Using the above Henry's Law constants along with the molecular weight, and an assumed average depth of 1 m of the body of water in equations 15-4, 15-5, 15-9 and 15-12 from Lyman et al. (1982), a range of half-lives of 1.2 days (using $H^1=1.1 \times 10^{-3}$) to

1.7 days (using H^1=1.6x10^{-8}) was estimated, which suggests that volatilization of propionitrile from water is significant. This prediction agrees with Lyman et al. (1982), who stated that volatilization of substances with a nondimensional Henry's Law constant of $\geq$4.0x10^{-4} is significant in all waters.

Sorption of propionitrile onto suspended particulate and organic matter is not expected to be very significant in view of the low K_{oc} value of 1.46.

2.3. SOIL

Pertinent data regarding the hydrolysis or other chemical reactions of propionitrile were not located in the available literature as cited in the Appendix. As in water, however, the hydrolysis of the cyano group should be very slow under normal environmental conditions.

Photochemical reactions of propionitrile at the soil surface are very unlikely (see Sections 2.1. and 2.2.), because absorption of light does not occur at $\geq$290 nm (Silverstein et al., 1981).

Biodegradation of propionitrile has been demonstrated by both a fungal strain and a bacterium isolated from soils (see Section 2.2.). Miller and Gray (1982) reported that the bacteria, Rhodococcus, utilizes propionitrile as the sole source of carbon and nitrogen. The rates of hydrolysis of propionitrile and its initial biodegradation product, propionamide, were shown to be 2.1$\pm$0.1 and 9100$\pm$1200 nmol ammonia produced/min/mg dry weight of cells, respectively. Kuwahara et al. (1980a) reported that the fungal strain, Fusarium solani MN7030, isolated from a soil sample and cultured in the laboratory, also used propionitrile as a source of carbon and nitrogen for growth. Kuwahara et al. (1980b) also reported that growth of Aeromonas sp. BN 7013 was supported by propionitrile. In view of these data, propionitrile in soil can be expected to biodegrade significantly.

Propionitrile from soil surfaces can be expected to volatilize significantly. This is based not only on the relatively facile volatilization of propionitrile from water but also on the very low estimated K_{oc} of 29 (see Section 1.2.).

Pertinent data regarding the leaching of propionitrile from soils were not located in the available literature as cited in the Appendix. Fielding et al. (1981), however, reported the detection of propionitrile in a sample of groundwater in a survey of various waters in the United Kingdom. No data on level were given and propionitrile was not detected in other groundwaters, nor in the other river and reservoir waters surveyed. The presence of propionitrile in one sample of groundwater suggests that leaching of propio- nitrile from the soil is at least possible. Furthermore, in view of the relatively high solubility of propionitrile in water and the low estimated K_{oc}, leaching of propionitrile from the soil may be significant, provided it is not biodegraded in soil.

3. EXPOSURE

Few data were located regarding the presence of propionitrile in the environment (see Appendix).

A National Organic Reconnaissance Survey (NORS) to determine the level of 72 organic contaminants including proprionitrile in drinking water from five selected cities in the United States was conducted by the U.S. EPA (Coleman et al., 1976). While no quantitative data were located regarding propionitrile itself, 1 of 6 nitriles was reported collectively to account for 8% of the total organic material consisting of the 72 organic compounds detected.

Fielding et al. (1981) reported that propionitrile was detected in a sample of groundwater in a survey of various waters in the United Kingdom. No concentration value or detection limits were reported and propionitrile was not detected in other groundwater tested, nor in the other river and reservoir waters surveyed.

Propionitrile has been detected in shale oil wastewaters (Hawthorne and Sievers, 1984; Sklarew and Hayes, 1984) (see Section 2.1.). The reports indicate that a large amount of the propionitrile p.esent is expected to be lost from the water as a result of volatilization (see Section 2.1.) unless the wastewater is stored or treated in closed containers. Propionitrile was detected but not quantified in two samples of ambient air collected near the oil shale wastewater treatment facility at the Logan, WA, site of Occidental Oil Shale, Inc. Propionitrile was not detected in an urban air sample in Boulder, CO, or in a rural air sample in an undeveloped area of the oil shale region. The detection limit reportedly was ~0.05 $\mu g/m^3$.

Sklarew and Hayes (1984) reported the presence of propionitrile in the offgas from a pilot oil shale retorting process. The levels detected ranged from 16-26 ppm (v/v) in the Rio Blanco vertical modified in situ retort 1.

Pellizzari et al. (1979) reported the presence of propionitrile in wastewaters produced during the manufacture of synthetic fuel by coal gasification. Product water from the Hanna II in situ coal gasification wells 5 and 6 in Hanna, WY, contained 382±47 µg/L propionitrile. Process water from an in situ coal gasification at Gillette, WY, contained levels of propionitrile of 175±22 µg/L. Retort water from the Omega-9 in situ oil shale processing plant at Rock Springs, WY, had levels of 27±7 µg/L propionitrile.

Monsanto (Keating, 1981) estimated airborne releases of propionitrile to be <75 pounds/day from its plants. Aqueous wastes from the Decater, AL, plant reportedly undergo biotreatment before being discharged into the Tennessee River; however, no tests to measure or detect atmospheric or aqueous discharge levels were reported.

Propionitrile has been found at 5 µg/L in the air surrounding turnip plants (Wallbank and Wheatly, 1976).

Propionitrile does not appear to have any consumer uses (U.S. EPA, 1983), and direct consumer exposure from industrially manufactured propionitrile is unlikely. Richter (1978) detected propionitrile in mainstream smoke from unfiltered cigarettes, and Jermini et al. (1976) detected 0.076 ppm propionitrile in sidestream smoke of cigarettes. Furthermore, propionitrile is released during incomplete combustion of nitrogen-containing materials during accidental fires (U.S. EPA, 1983). Anderson and Harland (1980) found propionitrile at levels up to 165 ng/mL in the blood of people killed by inhalation of smoke from fires (normal for nonsmokers is

2.8 ng/ml). Propionitrile was not determined recessarily to be the cause of death; furthermore, the levels of carboxyhaemoglobin from carbon monoxide poisoning were high enough to account for all fatalities.

Pertinent data regarding exposure to propionitrile from foodstuffs were not located in the available literature as cited in the Appendix.

Pertinent data regarding exposure of the general public to propionitrile through dermal contact were not located in the available literature as cited in the Appendix.

4. PHARMACOKINETICS

4.1. ABSORPTION

Silver et al. (1982) found ~65% of an orally administered dose of 0.75 mmol/kg of propionitrile as thiocyanate in the urine of rats collected over 24 hours. Very little thiocyanate was found in the next 24-hour period. These results indicated that at least 65% of the dose was absorbed by the gastrointestinal tract. Following oral treatment of rats with propionitrile at 40 mg/kg, blood cyanide levels rose from <0.5 µg/mL to 4 µg/mL within 1 hour (Ahmed and Farooqui, 1982). Levels of cyanide in the liver, kidney and brain were ~65, 17 and 500 times higher than control at 1 hour after dosing. Therefore, propionitrile was absorbed rapidly.

4.2. DISTRIBUTION

As indicated in Section 4.1., cyanide, a biotransformation product of propionitrile, was detected in brain, liver and kidney of rats within 1 hour of an oral dose of proprionitrile (Ahmed and Farooqui, 1982). Willhite and Smith (1981) detected cyanide in liver at 26.7±8 nmol/g wet wt. and in brain at 12.8±5.4 nmol/g wet wt. at 2.5 hours following intraperitoneal injection of mice with 28 mg/kg propionitrile (the LD_{50}). No cyanide was detected in the tissues of control mice. The brain cyanide level of mice was 0.72±0.13 µg/g tissue at 5.5 hours following an oral dose of 0.8 mmol/kg propionitrile (Tanii and Hashimoto, 1984a). Therefore, it appears that proprionitrile is broken down rapidly to cyanide, which is distributed to the brain; other tissues were not analyzed for cyanide or propionitrile levels.

4.3. METABOLISM

DeBruin (1976) presented a scheme for the biotransformation of proprionitrile (Figure 4-1). According to the scheme, hydroxylation of the alpha-carbon results in the formation of acetaldehyde cyanohydrin, which

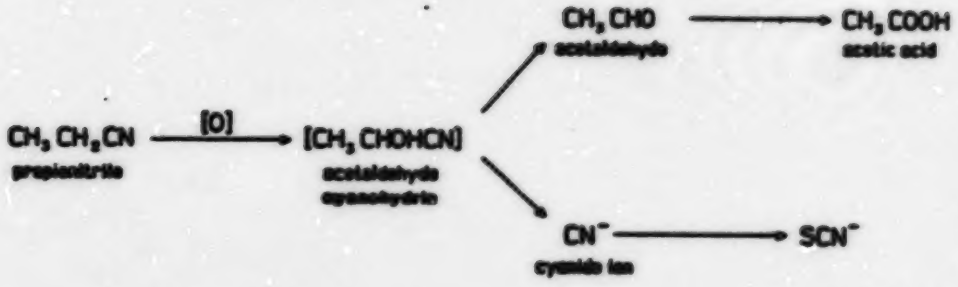

FIGURE 4-1

Generation of Cyanide Ion from Propionitrile

Source: DeBruin, 1976

dissociates into cyanide and acealdehyde. Cyanide, in turn, is converted to thiocyanate in a reaction catalyzed by rhodanese, and thiocyanate is excreted in urine.

Formation of the acetaldehyde cyanohydrin intermediate involves microsomal oxidation, as demonstrated *in vivo* by pretreatment of mice with carbon tetrachloride, an inhibitor of hepatic microsomal oxygenase (Willhite and Smith, 1981; Tanii and Hashimoto, 1984a,b) and *in vitro* using hepatic microsomal enzyme systems (Tanii and Hashimoto, 1984a,b). Willhite and Smith (1981) found that subcutaneous pretreatment of mice with carbon tetrachloride completely protected the mice against the lethality and toxic effects of an intraperitoneal dose of proprionitrile and reduced the brain cyanide levels. Similar results were obtained by Tanii and Hashimoto (1984a,b) in mice pretreated intraperitoneally with carbon tetrachloride before being treated orally with propionitrile. Tanii and Hashimoto (1984b) also studied the *in vitro* metabolism of proprionitrile using mouse liver microsomes. When pro- pionitrile at a concentration of 0.74 mM (5 times the K_m for the reaction) was incubated with microsomes from mice pretreated with olive oil, the rate of cyanide ion liberation was 1.44±0.22 ng CN^-/mg protein/minute; when microsomes from mice pretreated with carbon tetrachloride were used, no liberation of cyanide was detected.

4.4. EXCRETION

As indicated in Section 4.3., propionitrile is hydroxylated to a cyanohydrin intermediate which dissociates into cyanide and acetaldehyde. Cyanide is biotransformed into thiocyanate, which is excreted in the urine. Ghiringhilli (1956) found ~70% of the administered dose of propionitrile as thiocyanate in the urine of guinea pigs collected over 3 days following a subcutaneous injection of 15 mg/kg. The maximum urinary excretion was

essentially complete at 3 days. Silver et al. (1982) compared the excretion of thiocyanate following single doses of 0.75 mmol/kg propionitrile administered orally, intraperitoneally or intravenously. As indicated in Table 4-1, 46-65% of the dose was detected as thiocyanate in the urine collected over 24 hours. At 48 hours, ~70% of the oral dose was recovered as urinary thiocyanate.

TABLE 4-1

Urinary Excretion (24 hours) of Thiocyanate in Rats Dosed with 0.75 mmol (41.3 mg) of Propionitrile/kg[a,b]

Compound	Route	Number of Animals	Thiocyanate Excreted	
			mg/kg	% of Dose
Controls	NA	33	0.34±0.03	NA
Propionitrile	oral	5	28.7±1.3	65.1±2.9
	intraperitoneal	4	25.1±0.5	56.6±1.1[c]
	intravenous	3	20.4±1.9	46.0±4.4[c]

[a]Source: Silver et al., 1982

[b]Data expressed as mean± S.D.

[c]Significantly different ($p<0.05$) from the amount of thiocyanate excreted after oral administration

NA = Not applicable

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of propionitrile were not located in the available literature as cited in the Appendix, and this chemical is not scheduled for testing by the National Toxicology Program (NTP, 1985).

5.2. MUTAGENICITY

Propionitrile was tested for reverse mutations in S. typhimurium strains TA98, TA100, TA1535 and TA1537 (Florin et al., 1980). It was tested with or without metabolic activation using the S-9 fraction from Aroclor-induced rats. Propionitrile was not mutagenic in strains TA100, TA1535 and TA1537 when tested at 3 μmol/plate using the spot test. Negative results were also obtained when it was tested by plate incorporation at 0.03, 0.3, 3 and 30 μmol/plate in S. typhimurium strain TA98. Propionitrile was also negative for mutagenicity in Escherichia coli strain Sd-4-73 when tested at concentrations of 0.01-0.025 mL/plate (Szybalski, 1958). Canter (1983) reported that propionitrile has been scheduled for mutagenicity testing by the National Toxicology Program.

Arimoto et al. (1982) tested solvents, including propionitrile, used to dissolve test compounds for the Salmonella/mammalian microsome assay for their effect on the activity of tryptopyrolysate mutagen Trp-p-1. Propionitrile, in amounts of 25, 50 and 75 μL, was preincubated with Trp-p-1, S9 and Salmonella typhimurium strain TA98 and was found to have no enhancing effect toward the Trp-p-1 mutagen.

5.3. TERATOGENICITY

When administered intraperitoneally to pregnant golden hamsters, propionitrile induced malformations in the fetus and produced toxicity in the dam (Willhite et al., 1981a,b). Propionitrile was administered on day 8 of

gestation at doses of 0.54, 0.82 and 1.51 mmol/kg. Day 1 was defined as the day after mating. Other dams received two injections of 4.03 mmol/kg sodium thiosulfate intraperitoneally, one before and one following injection of propionitrile (Willhite et al., 1981a). All animals were sacrificed on day 14 of gestation for examination of fetuses. Propionitrile was maternally toxic at all doses, with death occurring in 3/8 dams treated with 0.54 mmol/kg. Mortality of dams treated with 0.82 or 1.51 mmol/kg was not reported. Treatment of the dams with sodium thiosulfate protected them against overt symptoms of nitrile poisoning that occurs when treated with propionitrile alone. As indicated in Table 5-1, propionitrile alone at 0.54 mmol/kg resulted in increased resorptions and abnormal fetuses. Abnormalities consisted of exencephaly and encephalo- coele. Results in fetuses of dams treated with 0.82 and 1.51 mmol/kg propionitrile alone were not reported. Injection of sodium thiosulfate prevented the production of malformations in the offspring of dams given 0.54 or 0.82 mmol/kg propionitrile, but failed to protect the embryos from teratogenic effects at 1.51 mmol/kg.

Histologic examination of embryos taken from hamster dams 10 hours after an interperitoneal injection of 0.54 mmol/kg propionitrile on day 8 of gestation revealed a reduction in the number of cells, shrinkage of cytoplasm, large extracellular spaces, reduced numbers of mitotic figures and focal necrosis in the mesoderm (Willhite et al., 1981b). The treated embryos had delayed development and failure of the neural folds to close.

Keating (1981), however, reported that propionitrile was not teratogenic to the offspring of groups of 25 female rats treated by gavage with 20, 40 and 80 mg/kg/day on days 6-19 of gestation. Additional details were not provided.

TABLE 5-1

The Effect of Intraperitoneal Injection of Propionitrile on Hamster Embryonic Development[a]

Treatment[b]	No. Litters	Implantation Sites	No. Resorptions (%)	No. Affected Litters (%)	No. Normal (%)	No. Abnormal (%)	Living Fetuses Abnormalities			
							Exencephaly	Encephalocoele	Ribs	Other[b]
0.9% NaCl (0.50 ml)	12	139	4 (2.8)	4 (33.3)	134 (99.2)	1 (0.8)	0	0	1	0
Propionitrile (0.54 mmol/kg) (30 mg/kg)	5	61	14 (22.9)	4 (80)	36 (76.6)	11 (23.4)	3	7	2	0
Propionitrile 0.54 mmol/kg $Na_2S_2O_3$ 8.06 mmol/kg[c]	4	53	0 (0)	0 (0)	53 (100)	0 (0)	0	0	0	0
Propionitrile 0.82 mmol/kg (45 mg/kg) $Na_2S_2O_3$ 8.06 mmol/kg[c]	5	71	0 (0)	0 (0)	71 (100)	0 (0)	0	0	0	0
Propionitrile 1.51 mmol/kg (83 mg/kg) $Na_2S_2O_3$ 8.06 mmol/kg[c]	5	57	0 (0)	2 (40.0)	51 (89.5)	6 (10.5)	1	2	3	0

[a]Source: Willhite et al., 1981a

[b]Includes facial cleft and crooked tail

[c]8.06 mmols/kg $Na_2S_2O_3$ = 1273 mg/kg of this compound

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5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of propionitrile were not located in the available literature as cited in the Appendix.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

No chronic studies of propionitrile were located; however, a 28-day drinking water study in rats (Sherr, 1983) and a 4-week inhalation study (Keating, 1981) were available in summary form.

An FYI submission (Sherr, 1983) to the Office of Toxic Substances included a 1953 report of a 28-day drinking water study. Groups of five male and five female albino rats were given propionitrile in the drinking water at concentrations of 0, 2.5, 12.5 and 62.5 mg/ℓ. Based on water consumption data, these concentrations were equivalent to dosages of 0, 0.32, 1.34 and 3.72 mg/kg/day, respectively. No significant differences were found in mortality, food consumption or body weight gain in rats treated at ≤12.5 mg/ℓ compared with controls. At 62.5 mg/ℓ, males and females had slightly reduced food consumption and appreciably reduced body weight gain, indicating a decreased efficiency of food utilization. One male rat died at 14 days; necropsy revealed hemorrhagic lungs.

In the inhalation study, an unspecified number of male and female rats were exposed to propionitrile at concentrations of 0.1, 0.16 or 0.75 mg/ℓ (100, 160 or 750 mg/m³) for 4 weeks (Keating, 1981). The duration and frequency of exposure were not reported. The only effects reported were 65% mortality in males and 5% mortality in females exposed to the highest concentration.

5.6. OTHER RELEVANT INFORMATION

Propionitrile has been shown to produce duodenal ulcers in rats treated orally or subcutaneously in short-term studies (Table 5-2), and at doses at, near or greater than the LD_{50} (Table 5-3); many of these studies were designed to investigate the mechanism of ulcerogenic response (see Table 5-2).

The acute toxicity of propionitrile is summarized in Table 5-3. Table 5-4 reports tests for skin and eye irritation.

TABLE 5-2

Short-term Toxicity of Propionitrile in Sprague-Dawley Rats

Route	Dose	Effect	Reference
Subcutaneous	6 mg/100 g on day 1 8 mg/100 g on day 2 15 mg/100 g on day 3 20 mg/100 g on day 4 3 times a day for 4 days	Rats developed duodenal ulcers on the 4th or 5th day of experiment. An unstated number of rats died on day 2 of exposure. These rats did not develop duodenal ulcers.	Szabo and Selye, 1972
Subcutaneous	20 mg/100 g on day 1 40 mg/100 g on day 2 50 mg/100 g on day 3 1 time a day for 4 days	Rats administered propionitrile once a day for 4 days showed lower incidence of duodenal ulcers than did those receiving a similar dose 3 times a day. Susceptibility to the ulcerogenic potential was age- and dose-related.	Szabo and Selye, 1972
Subcutaneous	6 mg/100 g on day 1 8 mg/100 g on day 2 10 mg/100 g on day 3 and 4	Duodenal ulcers in 80%; death in 100%; no adrenal necrosis	Szabo and Reynolds, 1975
Subcutaneous and oral	25, 50 and 75 mg/kg, 2 times a day for 2 days	At 50 mg/kg dose level, incidence of duodenal ulcers was maximum. Fasting of rats before and after treatment increased duodenal ulcers. 80% of females developed ulcers, while only 15% of the males did. At 75 mg/kg dose level, ulcer index was not significantly changed but mortality increased (67%).	Robert et al., 1975

TABLE 5-2 (cont.)

Route	Dose	Effect	Reference
Subcutaneous	6 mg/100 g on day 1 10 mg/100 g on day 2 20 mg/100 g on day 3	Rats were killed on day 4. Significant increase in gastric acid was observed. The authors state that enhanced gastric acid output may play an important role in the pathogenesis of propionitrile-induced duodenal ulcers.	Szabo et al., 1977
Subcutaneous	same as above	The formation of duodenal ulcers was prevented by vagotomy, decreased by sympathectomy, histamine depletion, histamine H-2 receptor antagonists, hypophysectomy, thyroidectomy and adrenalectomy. According to the author, antiulcerogenic effect of vagotomy, and histamine H-2 receptor antagonists are correlated with decreased gastric content. Cimetidine and metiamide exerted a dose-dependent antiulcer effect, but metamide enhanced mortality of rats.	Szabo et al., 1979
Subcutaneous	6 mg/100 g 2 times on day 1	Rats sacrificed at 2, 5 or 8 hours after the two injections. Earliest lesions in the duodenum became apparent at 5 hours in absorptive epithelial cells at tips of villus folds.	Giampaolo et al., 1975
Subcutaneous	15 mg/100 g on day 5; 20 mg/100 g on day 6	Adrenalectomy performed, day 1; ACTH (50 IU), day 2, 3 and 4. Toxicity of propionitrile was not prevented by ACTH in intact or adrenalectomized animals.	Szabo et al., 1973

TABLE 5-2 (cont.)

Route	Dose	Effect	Reference
Subcutaneous	10 or 15 mg/100 g	Toxic effect of propionitrile was slightly reduced by pregnenoline-16α-carbonitrile and triamcinolone, and not affected by surgical obstruction of the choledochus, partial hepatectomy and partial nephrectomy	Selye and Mecs, 1974a,b
Subcutaneous	6 mg/100 g on day 1 10 mg/100 g on day 2 20 mg/100 g on day 3	On day 3, metiamide was given orally at 10 mg/100 g 1 hour before administrattion of propionitrile.The frequency and intensity of propionitrile-induced duodenal ulcer was reduced 50% with metiamide but mortality was increased.	Dzau et al., 1975
	6 mg/100 g on day 1 10 mg/100 g on day 2 20 mg/100 g 3 times on day 3	Bilateral vagotomy performed 4 days before treatment or hypophysectomy performed 7 days before treatment. Vagotomy abolished occurrence of duodenal ulcer; hypophysectomy reduced the incidence and severity of the lesion.	Haith et al., 1975
Subcutaneous	6 mg/100 g	Rats had gastric fistulas and samples were taken 1, 2 and 4 hours after a dose. Propionitrile stimulated the gastric output of acid and pepsin.	Gallagher and Szabo, 1984a
Subcutaneous	6 mg/100 g	Rats had duodenal fistulas and samples were taken starting 1 hour after a dose. Propionitrile did not affect duodenal acidity. Duodenal ulcer incidence was 13% in propionitrile-treated rats.	Gallagher and Szabo, 1984b

TABLE 5-2 (cont.)

Route	Dose	Effect	Reference
Subcutaneous	5 mg/100 g	Animals treated with propionitrile had higher rates of HCO_3 secretion than controls. When the duodenal lumen was exposed to acid, the HCO_3 secretion was reduced by propionitrile. Propionitrile decreased the ability of the duodenal mucosa to maintain a high HCO_3, resulting in acidification of the surface epithelium.	Brid'en et al., 1985
Subcutaneous	5 mg/100 g	Dopamine-sensitive duodenal hypermotility induced by propionitrile. This interfaces with diffusion of pancreatic and biliary bicarbonate from the distal duodenum, leaving a large amount of gastric acid unneutralized in the duodenal bulb. Increased gastric acid output.	Szabo et al., 1984

TABLE 5-3

Acute Toxicity of Propionitrile to Laboratory Animals

Species	Route	Dose	Effect	Reference
Mouse	oral	35.8 mg/kg (26.9-47.7)*	LD_{50}	Tanii and Hashimoto, 1984a
	intraperitoneal	32 mg/kg	LD_{50}	Zeller et al., 1969
	intraperitoneal	33.7 mg/kg	LD_{50}	NIOSH, 1978
	intraperitoneal	28 mg/kg	LD_{50}: animals died in 1250 minutes	Willhite and Smith, 1981
	intraperitoneal	45 mg/kg	LD_{100}: animals died in 195 minutes	Willhite and Smith, 1981
	inhalation	163 ppm (367 mg/m³) 210 ppm (473 mg/m³) 400 ppm (901 mg/m³)	LC_{50} 80-90% mortality 100% mortality	Willhite, 1981
Rat	oral	39 mg/kg	LD_{50}	Smyth et al., 1951
	oral	80 mg/kg	LD_{50}	NIOSH, 1978
	oral	40 mg/kg	LD_{50}: caused convulsions, respiratory failure, CNS depression	Ahmed and Farooqui, 1982
	oral	64 mg/kg (44-93)*	LD_{50}: accelerated respiration and prostration	Sherr, 1983
	oral	180 mg/kg	LD_{50}	Zeller et al., 1969

TABLE 5-3 (cont.)

Species	Route	Dose	Effect	Reference
Rat (cont.)	oral	50-100 mg/kg		Fassett, 1963
	oral	75 mg/kg		Keating, 1981
	inhalation	500 ppm (1126 mg/m³), 4 hours	2/6 died	Smyth et al., 1951
	inhalation	air saturated with vapor, 2 minutes	100% mortality	Smyth et al., 1951
	inhalation	saturated vapors, ~120,000 mg/m³	100% mortality	Sherr, 1983
Rat	inhalation	3300 mg/m³, 4 hours	LC_{50}	Keating, 1981
	subcutaneous	150 mg/kg	LD_{50}	NIOSH, 1978
		6 mg/kg at 0 hours, repeat at 3 hours	At 8 hours: necrosis of villus folds in the duodenum.	Giampaolo et al., 1975
			At 24 hours: all animals showed duodenal ulcers.	
Rabbit	dermal	31.6-50.1 mg/kg	LD_{50}	Keating, 1981
		0.21 mL/kg, observed for 14 days		Smyth et al., 1951
		128 mg/kg (56-191)*	LD_{50}: 24-hour contact	Sherr, 1983

*Numbers in parentheses indicate the range.

TABLE 5-4

Skin and Eye Irritation Studies of Propionitrile in Laboratory Animals

Animal	Route	Dose	Effect	Reference
Rabbit	skin	unspecified amount on 2.5 cm^2 patch for 15 minutes to 20 hours	Slight to moderate irritation, vascularity	Zeller et al., 1969
		1.1-8.0 mg	Slight irritation	Keating, 1981
		NR	"Nonirritating." Least visible injection from undiluted material.	Smyth et al., 1951
	eye	NR	Necrosis on 63-87% of cornea. Severe eye injury.	Smyth et al., 1951
		one drop (50 mg)	Severe irritation, edema, slight necrosis	Zeller, 1969
		18.5-110 mg	Slight irritation	Keating, 1981
		0.1 mL for 10 seconds	Slight irritation	Sherr, 1983
Guinea pig	skin	NR	"Slightly irritating"	Fassett, 1963

NR = Not reported

6. AQUATIC TOXICITY

Few data regarding the toxic responses of aquatic organisms to propionitrile were located in the available literature as cited in the Appendix.

6.1. ACUTE TOXICITY

Indorato et al. (1983) investigated the toxicity of propionitrile to the fathead minnow, Pimephales promelas, and obtained a 96-hour LC_{50} value of 10 mg/ℓ. Crisp et al. (1967) reported observations of propionitrile producing narcotic effects in a species of barnacle, Elminius sp., larvae.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

NIOSH (1978) has recommended a TLV for occupational exposure to propionitrile of 14 mg/m³ (6 ppm) as a TWA concentration for a 10-hour work shift, 40-hour work week.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of propionitrile were not located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

No carcinogenic studies on propionitrile have been reported. Propionitrile was not mutagenic in Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 (Florin et al., 1980) or in Escherichia coli strain Sd-4-73 (Szybalski, 1958).

Propionitrile injected intraperitoneally in pregnant hamsters at ≥0.54 mmol/kg (30 mg/kg) on day 8 of gestation resulted in increased resorptions, exencephaly and encephalocoeles in fetuses (Willhite et al., 1981a). The intraperitoneal doses were also toxic to the dams resulting in deaths and signs of nitrile poisoning. Keating (1981), however, reported that propionitrile was not teratogenic following oral administration of rats at ≤80 mg/kg/day on days 6-19 of gestation.

Information regarding the effects of long-term exposure to propionitrile are limited. No significant differences were found in mortality, food consumption or body weight gain of rats maintained for 28 days on drinking water containing propionitrile at concentrations of 2.5 and 12.5 mg/ℓ (equivalent to 0.32 and 1.34 mg/kg/day, based on drinking water consumption data) (Sherr, 1983). At a concentration of 62.5 mg/ℓ (3.72 mg/kg/day), rats had slightly reduced food consumption and appreciably reduced body weight gain. One high-dose male died at 14 days and upon necropsy was shown to have hemorrhagic lungs. In an inhalation study, the only effects reported were 65% mortality in male rats and 5% mortality in female rats exposed to 750 mg/m³ propionitrile for 4 weeks (Keating, 1981). No effects were reported at the lower exposures of 100 or 160 mg/m³. The duration and frequency of exposure were not reported. The exposures of 12.5 mg/ℓ in the drinking water study and 160 mg/m³ in the inhalation study appear to

be NOELs. These studies, however, cannot be used to estimate an ADI for chronic exposure to proprionitrile because the only endpoints examined were mortality, weight gain and food consumption, and the durations of the studies were insufficiently long to approximate chronic exposure. Furthermore, in the inhalation study, a dose cannot be calculated because the duration and frequency of exposure were not reported.

Therefore, data are insufficient to derive a q_1^* or an ADI for propionitrile.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

No chronic or subchronic oral or inhalation studies of propionitrile were located; however, summaries of a 28-day drinking water study (Sherr, 1983), a 4-week inhalation study and a gavage teratogenicity study (Keating, 1981) in rats were available. These studies are summarized in Table 9-1. In the absence of information on the effects of chronic exposure to propionitrile, the short-term nature of the drinking water and inhalation studies precludes their use for deriving an RQ. Since no teratogenic or other effects in the gavage teratogenicity study were reported, an MED cannot be calculated from this study. Willhite et al. (1981a) reported that propionitrile was teratogenic to the offspring of pregnant hamsters treated intraperitoneally at $\geq$0.54 mmol/kg ($\geq$30 mg/kg) on day 8 of gestation (see Section 5.3.). Since no data comparing the effects of intraperitoneal and oral exposure of hamsters to propionitrile were available, however, it is not appropriate to derive an RQ based on the intraperitoneal teratogenicity study. Therefore, data are insufficient to derive an RQ for propionitrile (Table 9-2).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Pertinent data regarding the carcinogenicity of propionitrile in animals or humans were not located in the available literature as cited in the Appendix; therefore, the derivation of a potency factor is precluded. This chemical should be placed in IARC Group 3, since it cannot be classified regarding its carcinogenicity for humans.

TABLE 9-1

Oral and Inhalation Toxicity of Propionitrile in Rats[a]

Route	Sex	No. at Start	Vehicle/ Physical State	Dosage/ Exposure	Dose (mg/kg/day)	Response	Reference
Oral	M,F	5/sex/group	drinking water	2.5 and 12.5 mg/L, 28 days	0.32 and 1.36[b]	No effect on mortality, food consumption or body weight gain	Sherr, 1983
Oral	M,F	5/sex	drinking water	62.5 mg/L, 28 days	3.72[b]	Slightly reduced food consumption, appreciably reduced body weight gain; one male died and had hemorrhagic lungs	Sherr, 1983
Oral	F	25/group	gavage	20, 40, 80 mg/kg/day, days 6-19 of gestation	20, 40, 80	No teratogenic effects	Keating, 1981
Inhalation	M,F	NR	vapor	100 and 160 mg/m³ for 4 weeks	no dose calculated[c]	No effects reported	Keating, 1981
Inhalation	M,F	NR	vapor	750 mg/m³ for 4 weeks	no dose calculated[c]	65% mortality in males, 5% mortality in females	Keating, 1981

[a]Strain not reported

[b]The doses were based on drinking water consumption data.

[c]No dose could be calculated because the duration and frequency of exposure were not reported.

TABLE 9-2

Propionitrile

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:

Dose:

Effect:

Reference:

RV_d:

RV_e:

Composite Score:

RQ: Data are not sufficient for deriving an RQ

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CA SEARCH (Files 308, 309, 310, 311, 320
TOXLINE
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP

These searches were conducted in February, 1985. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. 486 p.

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Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

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Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

ITII (International Technology Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

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U.S. EPA. 1984. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982, USITC Publ. 1422. Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Resource Publ. 137. Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California. State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. PB-269605. Prepared for the U.S. EPA, Washington, DC.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. U.S. EPA, Office Pesticide Programs, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.